REMARKS

The Office Action dated July 30, 2003, has been received and reviewed. Claims 1-22 are pending in the present application. Claims 3-22 have been withdrawn from consideration by the Examiner as being drawn to a non-elected invention. Applicants confirm their election made during a teleconference with the Examiner with respect to Claims 3-22 with traverse. Claims 1-2 stand rejected. Claim 1 has been amended to recite due to an increase in HDL levels. Applicants respectfully request reconsideration of the application in view of the amendments to the claims and the arguments below.

I. Specification

The amendments to the Title and Specification are being made to correct grammatical and minor informalities.

Furthermore, applications note that the specification properly incorporates documents by reference. In paragraph 32, Applicants note that the documents cited refer to the previous sentence wherein it is stated, " Numerous different oligonucleotide probe assay formats are known which may be employed to carry out the present invention.". Furthermore, the references in paragraph 43 refers to the numerous estrogen replacement therapy preparations and protocols that are commonly known in the art. Accordingly, Applicants respectfully requests that this rejection be withdrawn.

II. Claim Rejections

A. 35 U.S.C. §112, first paragraph

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

Applicants note that the "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (MPEP §2164.01, citing *In re Wands*, 858 F.2d 731, 737). Furthermore, the test for whether or not the enablement requirement has been met involves determining whether or not practice of the invention as claimed involves "undue experimentation". It has long been settled that "the key word is 'undue', not 'experimentation'". *In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976). In the present case, Applicants submit that the application of the current technology requires routine effort, and not undue experimentation.

The Office Action alleges that the present specification has not provided evidence that the presence of these polymorphisms are found in other life forms, and that any of them has been shown to correlate with improved cardiovascular disease in women. Applicants note that the specification discloses that homozygotes for the less common intron 1 alleles experienced a 24% to 33% increase in HDL with HRT compared with a 13% increase in carriers of more common alleles. *See,* Paragraph 67. Furthermore, baseline HDL levels were slightly higher in IVS1-401 C/C and IVS1-1505 G/G women compared with women with the IVS1-401 T/T and IVS1-1505 A/A genotypes, respectively (P = 0.052 and 0.063). *See,* Paragraph 67. Additionally, in women on hormone replacement therapy with the IVS1-401 C/C genotype, HDL_3 levels increased by 13.6 mg/dl compared with 8.2 mg/dl in women with the C/T or T/T genotypes (P for interaction = 0.04). *See,* Paragraph 67. and Figure 3. Applicants note that it is well known in the art that an increase in HDL levels is favorable for cardiovascular health. Accordingly, Applicants submit that one of skill in the art could readily practice the invention as presently claimed in the application. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections to Claims 1 and 2.

B. 35 U.S.C. §112, second paragraph

Claims 1 and 2 also stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action alleges that the claims are indefinite as to what "constitutes 'a favorable response to estrogen replacement therapy with respect to cardiovascular health.'" Applicants have amended Claim 1 to further recite "due to increased HDL levels" to further define the claim. Additionally, Applicants note that the specification recites that "particularly with respect to cardiovascular health (*e.g.,* improved future cardiovascular health as compared to that found in the same patient without estrogen replacement therapy; a decreased probability of), heart disease (*e.g.,* a decreased , heart disease (*i.e.,* high density lipoprotein (HDL) level" the present method indicates a subject is "more likely to have a favorable response to estrogen replacement therapy." *See* Paragraph 10. Furthermore, the specification notes a favorable response with respect to cardiovascular health may be, for example, improved future cardiovascular health as compared to that expected in the same patient without estrogen replacement therapy; lack of an unduly deleterious effect on cardiovascular

health as compared to patients without the detected polymorphism. *See* Paragraph 23. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejections to Claims 1 and 2.

CONCLUSION

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

It is not believed that an extension of time and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,

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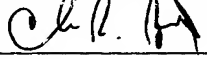

Clara R. Beard